American Journal of Hematology 52:212–214 (1996)

Lymphoblastic Transformation of Chronic Myelomonocytic Leukemia in an Infant

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A 10-month-old infant with chronic myelomonocytic leukemia (CMML) of 5 months' duration, who had been treated only with transfusion, displayed leukemic transformation characterized by lymphoid morphology, PAS positivity, and myeloperoxidase negativity. Surface marker analysis of blast cells revealed expression of lymphoid-associated antigens (CD10 and CD19) but not myeloid-associated antigens (CD13, CD14, and CD33). These findings suggest that some cases of infantile CMML are clonal disorders arising in a pluripotent stem cell that can also differentiate along the lymphoid cell lineage.

Key words: CMML, MDS, preleukemia, ALL, infantile leukemia

INTRODUCTION

Chronic myelomonocytic leukemia (CMML) characterized by morphological and functional abnormal hematopoiesis is classified as a myelodysplastic syndrome (MDS) according to the FAB classification system [1]. MDS occur mainly in elderly persons with a median age of approximately 70 years and are rare in children [2,3]. MDS are believed to be clonal stem cell disorders that often culminate in acute leukemia. With few exceptions [4,5], leukemia following MDS is generally of the acute myeloblastic variety [6]. We report here the case of an infant with CMML who underwent leukemic transformation to acute lymphoblastic leukemia (ALL).

CASE REPORT

A 5-month-old male infant was found to have hepatosplenomegaly in August 1993. He was born after normal pregnancy and delivery without a history of maternal irradiation or any toxic agents. There was no family history of malignancies or bleeding problems. Physical examination revealed a pale infant with marked hepatosplenomegaly. The liver was palpable 2 cm below the right costal margin and the spleen was palpable 7 cm below the left costal margin. There was no lymphoadenopathy or eczematoid rash and the remainder of the physical examination was unremarkable. The initial complete blood count was: red blood cells (RBC), 3.01×10^{12}/l; platelets, 91×10^{9}/l; and white blood cells (WBC), 16.7×10^{9}/l (43% neutrophils, 33% lymphocytes, 21% monocytes, 1% eosinophils, and 1% basophils). No blasts were seen in the peripheral blood. Bone marrow aspiration showed normocellular marrow, fewer than 1% blasts, and dysplastic features in the erythroid, granulocytic, and megakaryocytic lineages (Fig. 1A–C). Monocytes were increased in number and ringed sideroblasts were absent. The bone marrow karyotype was normal. Blood chemistry analysis revealed an increased HbF level (10%) and a normal serum level of muranidase and lactic dehydrogenase. He was diagnosed as having CMML according to the FAB classification and was followed up only with transfusion.

The patient remained generally well until 5 months after the onset of symptoms, when he presented with high fever, severe diarrhea, and remarkable splenomegaly. Blood count at that time was: RBC, 2.43×10^{12}/l; WBC, 7.2×10^{9}/l; with 8% blast cells, platelets, 38×10^{9}/l. Bone marrow showed 45.4% infiltration with blasts that had morphologic characteristics of lymphoblasts (Fig. 1D). Cytochemical staining of the blast cells revealed a number of PAS positive cells in which the staining pattern was granular, but no cells positive for myeloperoxidase,

Received for publication December 6, 1995; accepted January 18, 1996.

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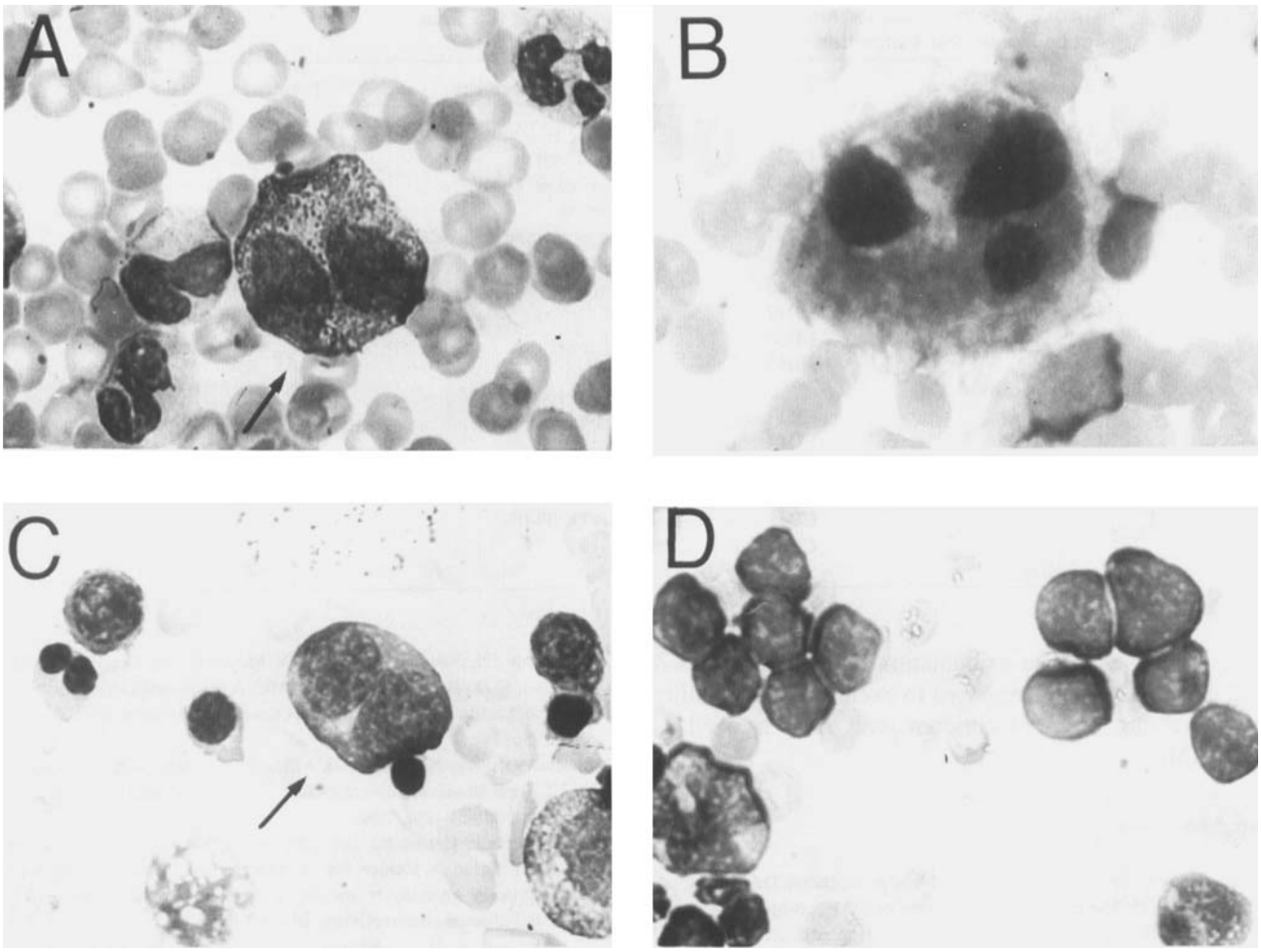

Fig. 1. Bone marrow smears (May-Grunwald-Giemsa stain) at the time of CMML (A, B, and C) and of leukemic transformation (D). A: Myelocyte with lobulated nuclei. B: Dysplastic megakaryocyte with polylobulation of the nuclei. C: Erythroblast with an abnormal lobulation. D: Predominance of lymphoblast-like cells.

alpha-naphthyl butyrate esterase, or naphthol AS-D chloroacetate esterase. The bone marrow karyotype was normal. Cell surface marker analysis of blast cells by flow cytometry (Table I) indicated expression of the lymphoid surface markers CD10 and CD19 and of HLA-DR in more than 75% of the cells, but essentially no expression of the myeloid surface markers CD13, CD14, or CD33. The patient was treated for lymphoblastic transformation with a low dose of cytosine arabinoside (Ara-C). Despite a marked decrease in the number of blast cells, no elevation of platelet count was observed. Repeat marrow examination showed fewer than 1% blasts but persistent myelodysplasia and hypocellularity. He is presently still on treatment.

DISCUSSION

The natural history, evolution, and prognosis of MDS in childhood has not been studied in detail, because of the relative rarity of the disease in young individuals. A previous study found that 17% of children with AML or 2.9% of all children with acute leukemia had a preleukemic presentation [7]. A more recent report suggests that, unlike adults, MDS in children run an aggressive clinical course and rapidly transform into AML irrespective of FAB subtype [8]. CMML particularly seems to bear a certain lineage fidelity in the transformation (monocytic or granulo-monocytic) [6]. In this report, we have described a case of infantile CMML that preceded overt leukemia with a lymphoid phenotype. To our knowledge, lymphoblastic transformation of CMML has not been described previously. In this case, the lymphoid antigen expression might reflect leukemic transformation of a pluripotent stem cell, which is capable of differentiating into lymphoid as well as myeloid cells.

The effect of cytotoxic chemotherapy in MDS is disappointing, with little effect on overall survival [8,9]. BMT presently remains the only curative treatment in these

TABLE I. Surface Marker Analysis of Marrow Blast Cells at the Time of Leukemic Transformation

Monoclonal antibody	Cluster	Antibody specificity	Positive cells (%)
Lymphoid marker			
OKT3	CD3	Mature T cell	1.4
OKT4	CD4	Inducer/helper T cell	1.8
OKT6	CD1	Thymocyte	6.2
OKT8	CD8	Suppressor/cytotoxic T cell	1.0
OKT11	CD2	ER-forming T cell	2.1
OKBcalla	CD10	CALLA	80.1
B4	CD19	Pan-B	75.6
B1	CD20	Pan-B	28.5
NKH-1	CD56	NK cell	0.4
Myeloid marker			
My7	CD13	Myeloid, monocyte	10.5
My4	CD14	Monocyte	6.4
My9	CD33	Myeloid	7.7
Others			
TP80	CD41	Platelet GPIIb/IIIa	0.9
My10	CD34	Stem cell	7.7
OKDR	—	HLA-DR	88.6

cases. Thus, a precise examination of peripheral blood and marrow smears is required to exclude the possibility of underlying MDS in children with ALL as well as with AML.

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